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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/529,205	Applicant(s) KATO ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-22,24 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-22,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1☒ Notice of References Cited (PTO-892)

4☐ Interview Summary (PTO-413) Paper No(s). _____

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 14 January 2002 (Paper No. 16) has been entered in full. Claims 8, 10, 12, 20-21, and 24 are amended and claims 23 and 26 are cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 7-22 and 24-25 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 2-3 of the previous Office Action (Paper No. 14, 13 August 2001) are *withdrawn* in view of the submitted abstract, amended title, and amended specification (Paper No. 16, 14 January 2002).

2. The rejection to claims 12, 20-22, and 24-25 under 35 U.S.C. § 112, second paragraph at pg 14-15 of the previous Office Action (Paper No. 14, 13 August 2001) are *withdrawn* in view of the amended claims (Paper No. 16, 14 January 2002).

3. The rejection to claims 8 and 12-19 under 35 U.S.C. § 102(b) and claims 20-22 and 24-25 under 35 U.S.C. § 102(b) at pg 15-16 of the previous Office Action (Paper No. 14, 13 August 2001) are *withdrawn* in view of the amended claims (Paper No. 16, 14 January 2002).

Claim Rejections - 35 USC § 101 and §112, first paragraph

4. Claims 7-22 and 24-25 are rejected under 35 U.S.C. 101 because the claimed invention is [illegible] specific and substantial asserted utility or a well established

experimentation. The basis for this rejection is set forth for claims 7-22 and 24-25 at pg 3-8 of the previous Office Action (Paper No. 14, 13 August 2001).

Claims 7-22 and 24-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth for claims 7-22 and 24-25 at pg 8-12 of the previous Office Action (Paper No. 14, 13 July 2001).

Claims 7-22 and 24-25 recite an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO: 11 that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 1 and an isolated nucleic acid comprising a nucleotide sequence that is at least 95% identical to the nucleotide sequence set forth in SEQ ID NO: 11. The claims also recite an isolated nucleic acid which encodes a fragment of a polypeptide wherein the fragment comprises at least 8 contiguous amino acids of SEQ ID NO: 1 and an isolated nucleic acid which encodes a naturally occurring allelic variant of the polypeptide consisting of the amino acid sequence of SEQ ID NO: 1. Furthermore, the claims recite an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 1 and an isolated polypeptide comprising a fragment of at least 8 contiguous amino acids of SEQ ID NO: 1. The claims are further directed to an expression system comprising the polynucleotide that produces the polypeptide, a recombinant host cell, a process of producing a recombinant host cell and polypeptide, and a method for preventing, treating, or ameliorating a medical condition by administering a

Applicant's arguments (Paper No. 16, 14 January 2002), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that a credible, specific, and substantial utility is apparent from the specification and the knowledge in the art at the time of Applicant's invention. Applicant contends that the specification teaches that the claimed nucleic acids, which were isolated from a cDNA library from human stomach cancer tissue, encode a polypeptide that is a transmembrane protein. Applicant argues that at the time the instant application was filed, those skilled in the art recognized that membrane proteins play important roles, such as signal receptors, ion channels, and transporters in the material transportation and the information transmission which are mediated by the cell membrane. Applicant states that Applicants developed a strategy to selectively identify and characterize those polynucleotides which encode for transmembrane proteins.

(ii) Applicant also asserts that the presently claimed nucleic acids and polypeptides (SEQ ID NO: 1 and SEQ ID NO: 11) are analogous to the chicken stem cell antigen 2 (Sca-2). Applicant indicates that Sca-2 is a member of the Ly-6 family of cell surface proteins. Applicant contends that as of the filing date of the application, the claimed polypeptides were known to be analogous to molecules belonging to a known family of membrane proteins. Applicant states Reiter et al. (Proc Natl Acad Sci USA 95: 1735-1740, 1998) describes a gene that is overexpressed in prostate cancer tissue, named prostate stem cell antigen (PSCA) based on its homology to Sca-2. Applicant asserts that the alignment of PSCA with the amino acid sequence set forth in SEQ ID

contends that these two polypeptides differ by a single amino acid and could be allelic variants of the same gene.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Applicant has not provided evidence to demonstrate that the polynucleotide and polypeptide of the instant specification have a specific and substantial asserted utility or a well established utility. Since the specification of the instant application does not disclose any methods or working examples that indicate the polynucleotide and polypeptide of the instant application exhibit similar activities of other membrane proteins, particularly Sca-2 or PSCA, the skilled artisan would not be able to categorize the polynucleotide and polypeptide of the instant application as a specific membrane protein. One skilled in the art would not know the utility and function of polypeptide of the instant application, even if it was a putative membrane protein because, as discussed in Applicant's response and the specification of the instant application, "membrane proteins play important roles, as signal receptors, ion channels, transporters, etc...Examples thereof include receptors for a variety of cytokines, ion channels of the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on" (pg 1, lines 22-27; pg 2, line 2) and neither the prior art nor the specification provides for the physiological significance of the disclosed and claimed protein. The skilled artisan would also not be able to characterize the polypeptide of the instant application and PSCA as variants of the same gene because PSCA is a prostate-specific gene that is overexpressed in more than 80% of prostate cancers. The polypeptide of the instant application is isolated from tissues of human

specification to indicate that the polypeptide of the instant invention is overexpressed or that it is present in any tissues other than stomach cancer.

The specification also does not teach a nucleic acid comprising a nucleotide sequence that is at least 95% identical to the nucleotide sequence set forth in SEQ ID NO: 11 or a nucleic acid molecule which encodes a polypeptide fragment comprising at least 8 contiguous amino acid residues of SEQ ID NO:1. Further, the specification does not teach an isolated polypeptide fragment comprising at least 8 contiguous amino acids of SEQ ID NO: 1. Additionally, the specification does not disclose functional or structural characteristics of the polynucleotides and polypeptides and any variants in the context of a cell or organism.

Applicant asserts that polypeptide of the instant application is homologous to an existing family of membrane proteins, such as Sca-2 and PSCA. However, the relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen *in vivo*, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see

(1996, PNAS USA 93:9602-9607) disclose that OP-1, a member of the TGF-β family of

proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF-β family (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid (column 2, lines 37-48).

Furthermore, the problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. Certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. Related literature, such as Spiegel (Annual Rev. Physiol. 58:143-170, 1995) and Pauwels et al. (Molec. Neurobiol. 17(1-3): 109-135, 1998) discuss gain-of-function and loss-of-function mutations in G protein-coupled receptors that cause a wide spectrum of hereditary and somatic disorders and diseases. For example, the ***single*** mutation of a lysine residue to a [illegible] position 296 in the rhodopsin receptor results in constitutive activation of

Applicant has provided little or no guidance beyond the mere presentation of sequence data to

enable one or ordinary skill in the art to determine, without undue experimentation, the positions in the protein and DNA which are tolerant to change and the nature and extent of changes that can be made in these positions.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotide to make the biologically active polypeptide of SEQ ID NO: 1 without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are. The regulation and sequestration of the polynucleotide and polypeptide of the instant application, are not well characterized and one skilled in the art the art would not find the utility of the polynucleotide of SEQ DI NO: 11 and polypeptide of SEQ ID NO: 1 to be well-established, well-known or obvious.

Additionally, the specification does not disclose methods or examples to enable one skilled in the art to obtain a "naturally occurring" polypeptide of SEQ ID NO: 1 or any allelic variants of SEQ ID NO: 1, particularly from other species besides human. The specification does not disclose the chromosomal locus for the human polynucleotide polypeptide of the instant application. Since allelic variants must be at the same locus as the gene (SEQ ID NO: 11), it would be undue experimentation for one skilled in the art to identify the locus and map variants to determine which are alleles.

disorders. However, the specification does not disclose any methods or working examples to

demonstrate that the polynucleotide and polypeptide prevent, treat, or ameliorate any medical condition in any mammalian subject. Undue experimentation would be required of the skilled artisan to determine the disease affected by altered levels or mutated forms of the polynucleotide and polypeptide (SEQ ID NO: 11 and SEQ ID NO: 1, respectively). Furthermore, a large quantity of experimentation would be required to determine the quantity administered, the best route of administration, the duration of treatment, and any possible side-effects.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide (SEQ ID NO: 1) such that it can be determined how to use the claimed polynucleotide (SEQ ID NO: 11) and to generate the derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular structural and functional limitations and also embrace a broad class of structural fragments and variants, undue experimentation would be required of the skilled artisan to make and or use the claimed invention in its full scope.

containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set for at pg 12-14 of the previous Office Action (Paper No. 14, 13 August 2001).

Claims 8, 10-20, and 24-25 are directed to an isolated nucleic acid comprising a nucleotide sequence that is at least 95% identical to the nucleotide sequence set forth in SEQ ID NO: 11. The claims also recite an isolated nucleic acid which encodes a fragment of a polypeptide comprising at least 8 contiguous amino acid residues set forth in the amino acid sequence of SEQ ID NO: 1. The claims are directed to an isolated nucleic acid molecule encoding a polypeptide consisting of a naturally occurring allelic variant of the polypeptide consisting of the amino acid sequence of SEQ ID NO: 1. Furthermore, the claims recite an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 1 and an isolated polypeptide comprising a fragment of at least 8 contiguous amino acids of SEQ ID NO: 1.

Applicant's arguments (Paper No. 16, 14 January 2002), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that, as discussed above, Applicant has identified a transmembrane protein with known characteristics. Applicant contends that the specification provides ample guidance for making and using nucleic acids and polypeptide within the scope of the pending claims.

Applicant's arguments have been fully considered but are not found to be persuasive

able to envision the detailed structure of the infinite number of polynucleotides and polypeptides

recited in the claims. The description of one human polynucleotide and polypeptide sequence in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mammalian variants and fragments. Therefore, only an isolated nucleic acid molecule (SEQ ID NO: 11) encoding a polypeptide (SEQ ID NO: 1), but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bridget E. Bunner
Art Unit 1647
March 4, 2002